



## PRACTICE

## RAPID RECOMMENDATIONS

# Transcatheter or surgical aortic valve replacement for patients with severe, symptomatic, aortic stenosis at low to intermediate surgical risk: a clinical practice guideline

In patients with symptomatic severe aortic stenosis but at lower risk of perioperative death, how do minimally invasive techniques compare with open surgery? Prompted by a recent trial, an expert panel produced these recommendations based on three linked rapid systematic reviews

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A randomised controlled trial of transcatheter aortic valve insertion (TAVI) versus surgical aortic valve replacement (SAVR) in patients with severe aortic stenosis was published in April 2016. The Partner 2 trial included 2032 people at intermediate surgical risk and favoured TAVI over open SAVR at two years for some outcomes.<sup>1</sup> It had the potential to change practice.

Before the availability of TAVI, the only effective treatment for symptomatic severe aortic stenosis was SAVR with mechanical or bioprosthetic valves (fig 1). In practice, patients offered mechanical valves tend to be younger and must accept lifelong anticoagulation. The minimally invasive option, TAVI, was developed for patients who are unfit for surgery, in whom its use is recommended by major US and European guidelines.<sup>2,3</sup>

Severe aortic stenosis affects approximately 3 in 100 people over the age of 75 years.<sup>4</sup> Patients typically experience symptoms of heart failure and reduced quality of life. Without aortic valve replacement, life expectancy is typically 50% at two years, with escalation of heart failure and reduced quality of life.<sup>5</sup> These recommendations are for patients with symptoms and severe aortic stenosis: patients without symptoms or with milder disease are not considered here. Box 1 shows the linked articles in this BMJ Rapid Recommendations cluster.

## How the recommendations were created

The international expert panel included front line and intervention cardiologists, a heart surgeon, internists, a general practitioner, methodologists, and people with lived experience of the condition (see list of panel members). To avoid bias, we excluded people with a professional, academic, or financial conflict of interest that we judged as excessive (see online methods supplement, competing interests statement, and appendix of interests of the panel members).

The panel followed standards for trustworthy guidelines and used the GRADE methodology to critically appraise the evidence and to create recommendations.<sup>6-8</sup> When moving from evidence to recommendations, the panel integrated information on benefits and harms of treatment alternatives, quality of evidence, and values and preferences of patients as well as acceptability, feasibility, and resources (see box 1). Estimates of absolute effects are derived from relative effect estimates from the systematic review coupled with the best population estimates of baseline risks derived from a linked systematic review of observational studies.<sup>9</sup> We label recommendations for or against each alternative as either weak or strong (see infographic).

## The evidence

A linked systematic review and meta-analysis combines the data from the Partner 2 trial with three other trials (see fig 2). It pools data on 3128 patients with symptomatic severe aortic stenosis at low or moderate risk of perioperative death, typically followed for two years.<sup>1-14</sup>

Compared with SAVR, transfemoral TAVI reduced mortality and stroke, life threatening bleeds, atrial fibrillation, and acute kidney injury at two years, but increased heart failure, major vascular complications, pacemaker insertion, and need for aortic valve reintervention within 2 years (see infographic).<sup>10</sup> In contrast, transapical TAVI may increase mortality and stroke compared with the surgical approach. The results for mortality, stroke, and acute kidney injury were based on a subgroup analysis for transfemoral versus transapical approach, deemed credible by the review authors according to specific criteria.<sup>15</sup>

Estimates of baseline risk for most outcomes came from a linked systematic review on prognosis for patients undergoing SAVR.<sup>9</sup>

The panel were reasonably confident that the absolute effect sizes for the short term benefit and harm of TAVI and SAVR were true and accurate estimates (that is, overall moderate certainty according to GRADE). But the panel were very uncertain about the long term durability of the valves used in TAVI, particularly with respect to their recommendations in younger patients with a longer predicted life expectancy. The low certainty in the estimated long term re-intervention rate after TAVI of approximately 27 in 100 people reflects an absence of published follow-up studies beyond five years.

The linked systematic review on values and preferences yielded extremely limited evidence to inform the recommendations, particularly their strength.<sup>16</sup> There are no studies on patients deciding between TAVI and SAVR, although one study evaluated patient preferences and values when deciding whether to undergo SAVR (versus no surgery).<sup>16,17</sup> One study identified multiple biomedical, functional, social, and environmental factors influencing patients' decisions to undergo assessment for TAVI.<sup>18</sup> Overall, there is evidence of variability in individual values and preferences, highlighting the need for shared decision making, particularly for patients aged between 65 and 85 years.

## Practical considerations

Perioperative risk is typically assessed by expert cardiovascular teams. Validated risk scores such as the STS-PROM are available online ([www.riskcalc.sts](http://www.riskcalc.sts)).

Type of device and TAVI approach may vary: balloon expandable and self expanding devices can be used via

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Data supplements on [bmj.com](http://bmj.com) (see <http://www.bmj.com/content/354/bmj.i5085?tab=related#datasupp>)

Infographic: Summary of recommendations and evidence

Appendix 1: Full list of authors' declarations of interests

Appendix 2: Methodology for development of *BMJ* Rapid Recommendations

Appendix 3: The full information available on the MAGICapp

Appendix 4: Rapid Recommendation panel members

**What you need to know**

- New trial evidence confirms that transcatheter aortic valve insertion (TAVI), initially developed for patients with severe aortic stenosis who were unfit for surgical aortic valve replacement (SAVR), can be offered also to patients at low to intermediate surgical risk
- Long term durability of TAVI valves remains highly uncertain
- Age stratified recommendations reflect that TAVI is probably preferable to those over 75 years old, whereas SAVR is likely preferable to those under 75 years

**Box 1: Linked articles in this BMJ Rapid Recommendations cluster**

- Siemieniuk RA, Agoritsas T, Manja V, et al. Transcatheter versus surgical aortic valve replacement in patients with severe aortic stenosis at low and intermediate risk: systematic review and meta-analysis. *BMJ* 2016;354:i5130. doi:10.1136/bmj.i5130
- Foroutan F, Guyatt GH, O'Brien K, et al. Prognosis after surgical replacement with a bioprosthetic aortic valve in patients with severe symptomatic aortic stenosis: systematic review of observational studies. *BMJ* 2016;354:i5065. doi:10.1136/bmj.i5065
- Lytvyn L, Guyatt GH, Manja V, et al. Patient values and preferences on transcatheter or surgical aortic valve replacement therapy for aortic stenosis: a systematic review. *BMJ Open* 2016;6:e014327. doi:10.1136/bmjopen-2016-014327
- Editorial: Siemieniuk RA, Macdonald H, Agoritsas T, Guyatt GH, Vandvik PO. Introduction to BMJ Rapid Recommendations. *BMJ* 2016;354:i5191. doi:10.1136/bmj.i5191.
- Magic App ([www.magicapp.org/public/guideline/aEeKpL](http://www.magicapp.org/public/guideline/aEeKpL))
  - Expanded version of the results with multilayered recommendations, evidence summaries, and decision aids for use on all devices

transfemoral, subclavian, direct aortic, transcarotid, or transapical (balloon only) routes.

Fig3<sup>1</sup> lists issues that may influence a person's choice of procedure. These are further detailed in MAGICapp within the consultation decision aids that provide all desirable and undesirable consequences of treatment options.

**Costs and resources**

There are no cost effectiveness data for patients at low to intermediate surgical risk considering TAVI versus SAVR. Both procedures are resource demanding and require an experienced cardiovascular team (table 1<sup>1</sup>). In general, TAVI devices are more expensive than surgery, but this extra cost may be partially offset by a slightly shorter hospital stay and less need for post-discharge rehabilitation.

**Future research**

Future recommendations and guidelines would benefit from studies that answer the following questions

- Qualitative or survey study. What are the values and preferences of patients deciding between TAVI and SAVR, particularly with respect to uncertain durability of TAVI devices, the desire to avoid open heart surgery, and post-procedure pain and recovery time?
- What is the durability of the TAVI valves beyond five years?

**Competing interests:** All authors have completed the *BMJ* Rapid Recommendations interests form. The *BMJ* Rapid Recommendations team judged that no panel member declared financial, professional, or academic interests that precluded authorship. The declared interests for each panel member are attached. No panel members declared any financial conflicts of interest related to this clinical question, specifically no financial ties to the heart valve industry. D Brieger receives personal and institutional research funding from industry, none relevant for TAVI or SAVR (has received funding from Eli Lilly, Astra Zeneca, Sanofi Aventis, Boehringer Ingelheim, Pfizer, Merck Sharp and Dohme, Bristol-Myers Squibb, and Bayer all related to antithrombotic or diabetes therapy). R Whitlock has received funding for consulting with Atricure and Armethon (both focus on atrial fibrillation management). R Bagur is a primary investigator of a trial on anticoagulation in atrial fibrillation, sponsored by Bristol-Myers Squibb. R Whitlock performs SAVR. R

Bagur performs TAVI. CM Otto has co-chaired the American College of Cardiology guidelines on valvular heart disease, which includes TAVI, and is the UpToDate editor on the same topic. R Whitlock is the section lead for the American College of Chest Physicians valve guidelines. S Price is a panel member of the European Cardiology Society guidelines on heart valves. RA Siemieniuk, GH Guyatt, PO Vandvik, CM Otto, R Bagur, F Foroutan, and L Lytvyn participated in writing the complementary systematic reviews that formed the evidence base for this guideline. No panel member has previously formally made statements favouring either option in low or intermediate perioperative risk patients. This article was edited by H MacDonald at *The BMJ* who had no relevant financial or intellectual interests.

- 1 Leon MB, Smith CR, Mack MJ, et al. PARTNER 2 Investigators. Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients. *N Engl J Med* 2016;374:1609-20. doi:10.1056/NEJMoa1514616 pmid:27040324.
- 2 Nishimura RA, Otto CM, Bonow RO, et al. ACC/AHA Task Force Members. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014;129:2440-92. doi:10.1161/CIR.000000000000029 pmid:24589852.
- 3 Vahanian A, Alfieri O, Andreotti F, et al. Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) European Association for Cardio-Thoracic Surgery (EACTS). Guidelines on the management of valvular heart disease (version 2012). *Eur Heart J* 2012;33:2451-96. doi:10.1093/eurheartj/ehs109 pmid:22922415.
- 4 Osnabrugge RL, Mylotte D, Head SJ, et al. Aortic stenosis in the elderly: disease prevalence and number of candidates for transcatheter aortic valve replacement: a meta-analysis and modeling study. *J Am Coll Cardiol* 2013;62:1002-12. doi:10.1016/j.jacc.2013.05.015 pmid:23727214.
- 5 Otto CM. Timing of aortic valve surgery. *Heart* 2000;84:211-8. doi:10.1136/heart.84.2.211 pmid:10908267.
- 6 Laine C, Taichman DB, Mulrow C. Trustworthy clinical guidelines. *Ann Intern Med* 2011;154:774-5. doi:10.7326/0003-4819-154-11-201106070-00011 pmid:21646561.
- 7 Guyatt GH, Oxman AD, Vist GE, et al. GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924-6. doi:10.1136/bmj.39489.470347.AD pmid:18436948.
- 8 Alonso-Coello P, Oxman AD, Moher J, et al. GRADE Working Group. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 2: Clinical practice guidelines. *BMJ* 2016;353:i2089. doi:10.1136/bmj.i2089 pmid:27365494.
- 9 Foroutan F, Guyatt GH, O'Brien K, et al. Prognosis after surgical replacement with a bioprosthetic aortic valve in patients with severe symptomatic aortic stenosis: systematic review of observational studies. *BMJ* 2016;354:i5065. doi:10.1136/bmj.i5065.
- 10 Siemieniuk RA, Agoritsas T, Manja V, et al. Transcatheter versus surgical aortic valve replacement in patients with severe aortic stenosis at low and intermediate risk: systematic review and meta-analysis. *BMJ* 2016;354:i5130. doi:10.1136/bmj.i5130.
- 11 Nielsen HH, Klaaborg KE, Nissen H, et al. A prospective, randomised trial of transapical transcatheter aortic valve implantation vs. surgical aortic valve replacement in operable elderly patients with aortic stenosis: the STACCATO trial. *EuroIntervention* 2012;8:383-9. doi:10.4244/EIJV8I3A58 pmid:22581299.
- 12 Adams DH, Popma JJ, Reardon MJ, et al. U.S. CoreValve Clinical Investigators. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med* 2014;370:1790-8. doi:10.1056/NEJMoa1400590 pmid:24678937.
- 13 Søndergaard L, Steinbrüchel DA, Ihlemann N, et al. Two-year outcomes in patients with severe aortic valve stenosis randomized to transcatheter versus surgical aortic valve replacement: the All-Comers Nordic Aortic Valve Intervention Randomized Clinical Trial.

### How patients were involved in the creation of this article

Two people with lived experience of severe aortic stenosis were full panel members and contributed with their experience and perspectives throughout the Rapid Recommendations process. Initially the community panel members identified pain and recovery time (in addition to already identified outcomes) and practical issues as important for choosing between TAVI and SAVR. They also fully participated in teleconferences and email exchange to discuss the evidence, draft recommendations, and to provide feedback in the creation of this article.

*Circ Cardiovasc Interv* 2016;9:e003665. doi:10.1161/CIRCINTERVENTIONS.115.003665 pmid:27296202.

- 14 Thyregod HG, Steinbrüchel DA, Ihlemann N, et al. Transcatheter versus surgical aortic valve replacement in patients with severe aortic valve stenosis: 1-year results from the All-Comers NOTION Randomized Clinical Trial. *J Am Coll Cardiol* 2015;65:2184-94. doi: 10.1016/j.jacc.2015.03.014 pmid:25787196.
- 15 Sun X, Briel M, Walter SD, Guyatt GH. Is a subgroup effect believable? Updating criteria to evaluate the credibility of subgroup analyses. *BMJ* 2010;340:c117. doi:10.1136/bmj.c117 pmid:20354011.
- 16 Lytvyn L, Guyatt GH, Manja V, et al. Patient values and preferences on transcatheter or surgical aortic valve replacement therapy for aortic stenosis: a systematic review. *BMJ Open* 2016;6:e014327. doi:10.1136/bmjopen-2016-014327.
- 17 Lauck SB, Baumbusch J, Achtem L, et al. Factors influencing the decision of older adults to be assessed for transcatheter aortic valve implantation: An exploratory study. *Eur J Cardiovasc Nurs* 2015;1474515115612927.pmid:26498908.
- 18 Hussain AI, Garratt AM, Brunborg C, Aakhus S, Gullestad L, Pettersen KI. Eliciting patient risk willingness in clinical consultations as a means of improving decision-making of aortic valve replacement. *J Am Heart Assoc* 2016;5:e002828. doi:10.1161/JAHA.115.002828 pmid:26994130.

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## Table

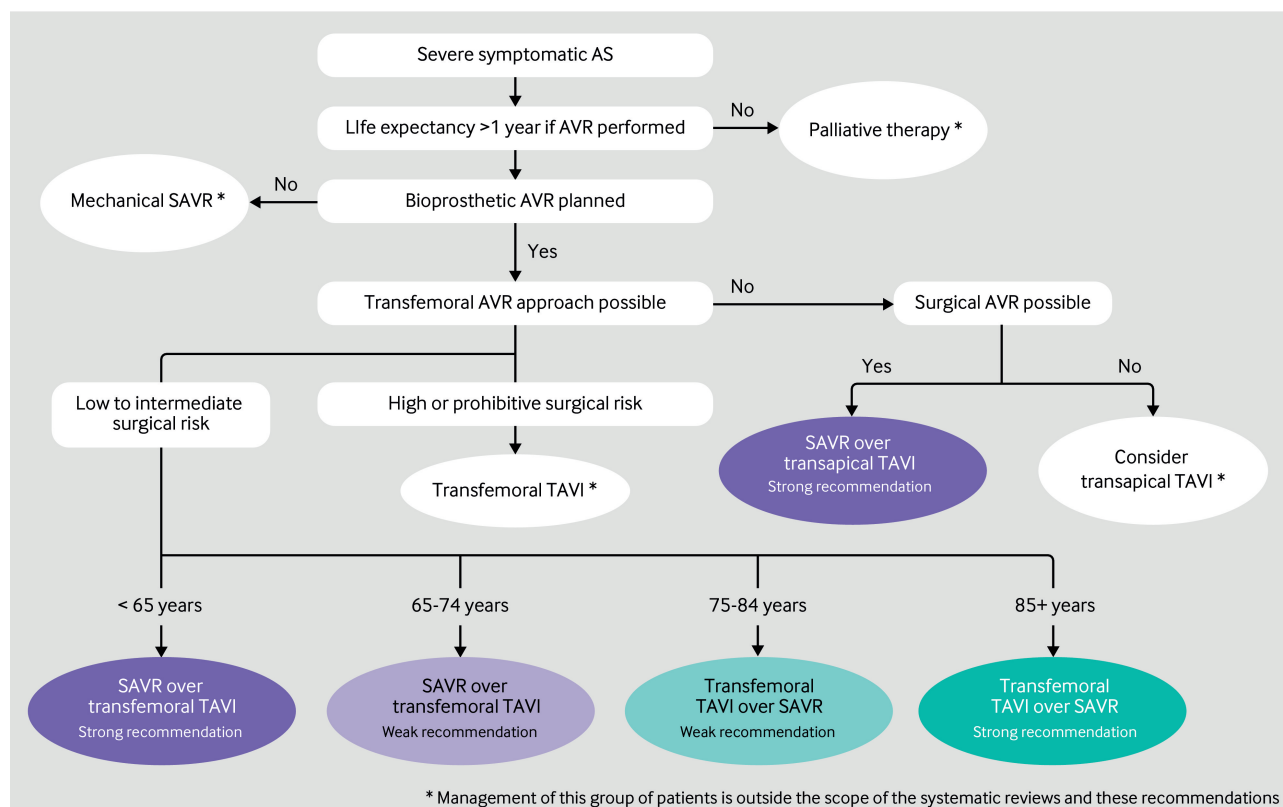
**Table 1 | Facilities and teams required for transcatheter aortic valve insertion (TAVI) versus surgical aortic valve replacement (SAVR)\***

Resource	Extent of requirement	
	TAVI	SAVR
Heart team	+++	++
Surgical backup	+++	N/A
Cardiac anaesthesia	+++	+++
Hybrid suite	++	—
Catheterisation laboratory facility	+++	+
Intensive care unit	++	+++
Coronary care unit	++	+/-
Length of hospital stay (days)†	2-5	5-10
Rehabilitation	++	+++
Follow-up clinic	++	++

\*Based on panel expert members experience from practice.

†Estimates reflect current practice according to content experts on the panel. Length of stay was considerably longer in the trials (see infographic).

## Figures



**Fig 1** Flowchart for management of severe aortic stenosis (AS). Coloured boxes represent the recommendations covered by this article. AVR=aortic valve replacement, SAVR=surgical aortic valve replacement, TAVI=transcatheter aortic valve insertion

## Patient and trial characteristics



**Fig 2** Patient and trial characteristics in the four trials of the linked meta-analysis<sup>10</sup>

**Fig 3** Practical considerations that may influence a patient's choice of procedure. For a complete list, see decision aids in the MAGICapp ([www.magicapp.org/public/guideline/aEeKpL](http://www.magicapp.org/public/guideline/aEeKpL))